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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/811,410	03/20/2001	Rudi Scherhag	0480/01227	1484

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EXAMINER	
SNEDDEN, SHERIDAN	

ART UNIT	PAPER NUMBER
1653	15

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/811,410	Applicant(s) SCHERHAG ET AL.	
	Examiner Sheridan K Snedden	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. This Office Action is in response to Paper No: 12, filed 4 March 2003. Claim 6 has been canceled. Applicant's amendment of claims 1, 3, 5, 8, and 10 is acknowledged. Applicant's addition of new claim 12 is acknowledged. Claims 1-5 and 7-12 are under examination.

Withdrawal of Objections and Rejections

2. The objections and/or rejections not explicitly restated or stated below are withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 5, and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite as to the use of "at least about" because it is unclear whether the limitation should read "a least 4" or "about 4." See same issue in claim 11.

Claim 5 is dependent on claim 4 and does not clear up the ambiguity.

4. Applicant argues that the "at least about" language is clear. However, it is unclear whether the limitation is "at least 4," "about 4," "at least 3," etc. and as such the meets and bounds of the claims limitation is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-5 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Kurfuerst *et al.* (US Patent 5,663,141). Kurfuerst *et al.* teach a method of preventing coagulation of blood by administration to a host a PEG-hirudin conjugate (see claim 13; regarding claim 1). Kurfuerst *et al.* teach that the PEG-hirudin are useful for the prophylaxis of thromboembolic disease and for extracorporeal circulation, e.g. hemodialysis (see column 5, lines 30-52; regarding claim 2). Kurfuerst *et al.* teach that the compounds are administered as a daily dose between 20 to 40,000 ATU/kg body weight (see column 5, lines 55-60; regarding claim 3). Kurfuerst *et al.* teach that the PEG-hirudin conjugates are superior to hirudin and heparin due to the prolonged biological activity (half-life), better bioavailability, and lower antigenicity (see column 5, lines 30-52). As such, the PEG-hirudin conjugates taught by Kurfuerst *et al.* display the 'enduring' activity necessitated in claim 5 and possess the inherent characteristic of a half-life of about 4 hours (regarding claim 4). The PEG-hirudin conjugate taught by Kurfuerst *et al.* is recombinant (see Example 1; regarding claim 12). Thus, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-5 and 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurfuerst *et al.* (US Patent 5,663,141) in view of Maraganore *et al.* (US Patent 5,256,559), De Rosa *et al.* (US Patent 5,723,576) and Fischer *et al.* (Kidney Int Suppl. 1999 Nov;72:S46-50).

Kurfuerst *et al.* teach a method of preventing coagulation of blood by administration to a host a PEG-hirudin conjugate (see claim 13; regarding claim 1). Kurfuerst *et al.* teach that the PEG-hirudin are useful for the prophylaxis of thromboembolic disease and for extracorporeal circulation, e.g. hemodialysis (see column 5, lines 30-52; regarding claim 2). Kurfuerst *et al.* teach that the compounds are administered as a daily dose between 20 to 40,000 ATU/kg body weight (see column 5, lines 55-60; regarding claim 3). Kurfuerst *et al.* teach that the PEG-hirudin conjugates are superior to hirudin and heparin due to the prolonged biological activity (half-life), better bioavailability, and lower antigenicity (see column 5, lines 30-52). As such, the PEG-hirudin conjugates taught by Kurfuerst *et al.* display the 'enduring' activity necessitated in claim 5 and possess the inherent characteristic of a half-life of about 4 hours (regarding claim 4). The PEG-hirudin conjugate taught by Kurfuerst *et al.* is recombinant (see Example 1; regarding claim 12).

Maraganore *et al.* teach the use of PEG-hirudin compositions which display the anticoagulant and platelet inhibitory activities for therapeutic and prophylactic purposes (see abstract, Example 12, column 9, lines 1-19). Inhibition of platelet aggregation may also be desirable in extracorporeal treatments of blood, such as dialysis, storage of platelets in platelet concentrates and following certain surgical procedures, such as heart-lung bypass (see column 2, lines 1-9). The PEG-hirudin conjugates are administered to a host with a single dose (see column 10, lines 59-68). As such, the PEG-hirudin conjugates taught by Maraganore *et al* display the

'enduring' activity necessitated in claim 5 and possess the inherent characteristic of a half-life of about 4 hours (regarding claim 4; see example 12). Recomdinant DNA technologies may be utilized to supply the needed hirudin in order to make PEG-hirudin (see column 4, line 40).

De Rosa *et al.* teach the use of hirudin derivatives as an anticoagulant and antithrombotic agents (column 2, lines 4-5) useful for therapeutic, prophylactic and diagnostic applications. De Rosa *et al.* specifically teach the use of hirudin derivative compounds, in the prophylaxis of vascular complication such as arterial thrombosis, and specifically teach the use of the above compounds in extracorporeal circulation, particularly hemodialysis (column 7, lines 49-57). De Rosa *et al.* teach that the above compounds can be administered to a patient with the effective amount of 0.05 mg/kg to 250 mg/kg patient body weight per day (column 7, lines 19-37) and teach that administration of the anticoagulant hirudin derivates prolong APTT 250%, or 2.5 fold (column 10, line 60).

Kurfuerst *et al.* teaches that the PEG-hirudin has superior qualities to other anticoagulants, such as other hirudin and heparin derived compounds. Therefore, the teachings of Kurfuerst *et al.* would suggest and motivate one of ordinary skill in the art to substitute the PEG-hirudin compounds with other anticoagulants for use as prophylaxis of thromboembolic disease and for extracorporeal circulation (e.g. hemodialysis) as taught by Kurfuerst *et al.* and Maraganore *et al.*. Administration of anticoagulants, such as hirudin, heparin or PEG-hirudin, in the form of a single dose prior to the start of hemodialysis is the standard of the prior art (regarding claims 8-9). Additionally, the anticoagulants are utilized in chronic treatments (regarding claims 7, 11). These standard protocols are exemplified by the teachings of Fischer *et al.* that demonstrate the single bolus of hirudin was use for patients undergoing continuous

hemodialysis for treatment of chronic renal failure. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute hirudin in the treatment taught by Fischer *et al.* with PEG-hirudin as suggested by Kurfuerst *et al.* The teachings of De Rosa *et al.* indicate that the PEG-hirudin compounds would posses the inherent activity to prolong APTT by at least 2.5 fold (regarding claims 10-11). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Advisory Information

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-3975 for regular communications and (703) 746-3975 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
May 19, 2003
SKS

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER